Whitepaper

The future of chemicals is Safe and Sustainable by Design

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TNO innovation for life

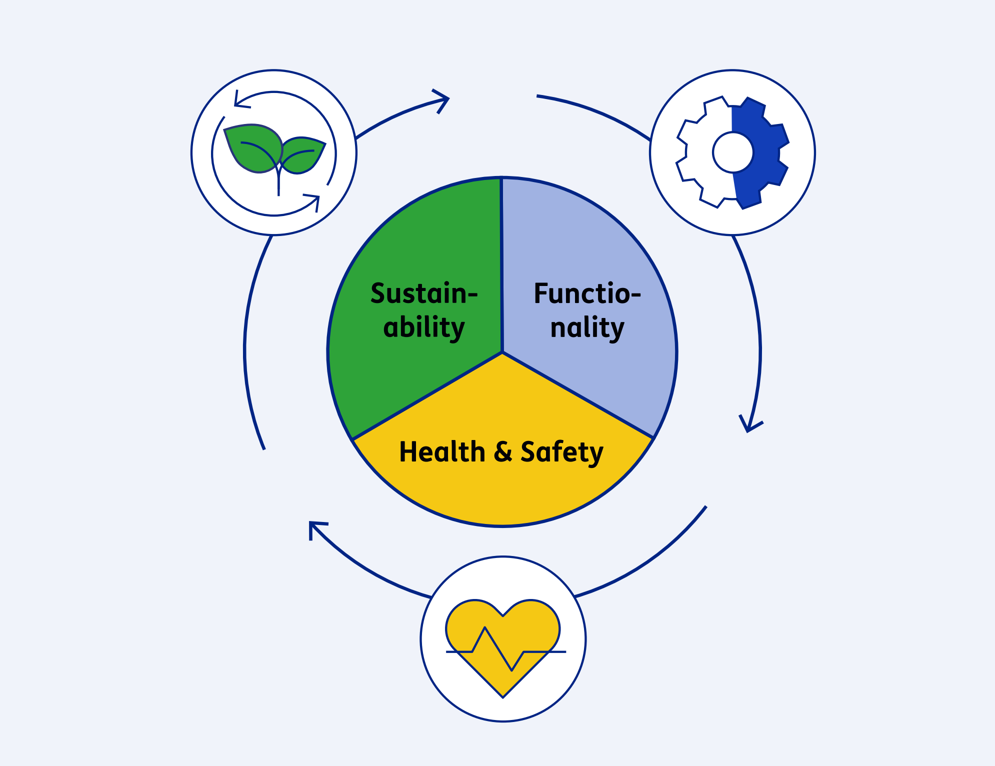
Summary

Every day, we encounter a myriad of chemicals and materials present in the products we use, with the demand for these substances steadily increasing each year. The constant innovation in designing novel chemicals and materials, however, comes with potential risks. The production, use, and disposal of these substances can have adverse effects on both human health and the environment.

Addressing health, safety and sustainability early during product innovation is part of the Safe and Sustainable by Design (SSbD) paradigm. SSbD is a pivotal element of the Chemicals Strategy for Sustainability published by the European Commission to move towards a safer, healthier, and more sustainable future. This strategy aims to transition to a circular economy that is safe, climate-neutral, and sustainable. TNO aims for a paradigm shift where safety and sustainability considerations are integrated at the earliest stages of product development, running parallel to functionality and cost considerations. This proactive approach allows for the identification of potential opportunities to enhance safety and sustainability early in the innovation process. By doing so, companies have the flexibility to adapt their products, minimizing adverse effects and mitigating the risk of market failure.

Despite the current European Chemicals legislation (REACH), adverse effects are often discovered late in the product development cycle. In some cases, adverse effects only become apparent years after market approval, resulting in disastrous consequences for society and the environment (e.g. PFAS), and leading to financial burdens for companies and potential reputational damage. TNO contends that SSbD presents an opportunity to proactively design innovative chemicals and materials that not only provide solutions to societal challenges, such as the energy transition, but also ensure no harm is caused to humans or the environment – embodying the principles of being safe and sustainable by design.

TNO assists industry in achieving this delicate balance between substance functionality, safety, and sustainability by developing an integrated approach during the early phases of product innovation. The TNO approach includes: 1) defining criteria for functionality, safety and sustainability; 2) quick screening of the selected aspects and criteria; 3) transparent visualisation of the SSbD aspects; 4) evaluation and decision support. TNO develops a Decision Support System with the collaboration of manufacturing industries, innovators, researchers, and governments.



Enabling safe and sustainable innovation of novel chemicals, materials and products

Such a system empowers industries to effectively balance risks and benefits in the early stages of their design process, contributing to the creation of a healthier and more sustainable society.

Contents

The challenges of our chemical-dependant society

Chemicals are all around us

In our daily lives, we find ourselves surrounded by a multitude of chemicals and materials, ranging from household products used for cleaning to the clothes we wear and the electronic devices we use. The continuous growth in world population and increasing living standards have led to a rising demand for chemicals, materials, and products[1] year after year. The market sees a constant influx of new chemicals and products, particularly in the fields of energy, electronics, construction, and biomaterials, where innovative substances are essential and designed at an accelerated pace. Globally, the chemical industry stands as the second-largest manufacturing sector and continues to grow rapidly.[2] From 1950 to 2010, global chemical production experienced a fiftyfold increase.[3] Projections for 2025 anticipate the global chemicals market to reach an impressive 4,304 billion dollars.

Our health and biodiversity are at threat

While many chemicals have beneficial uses and contribute positively to our lives, there can also be harmful side-effects on our health and the environment. The World Health Organization (WHO) assesses the overall impact of diseases by considering the number of years lost due to illness, disability, or premature death. For 2019, the WHO estimated that diseases related to chemicals caused a burden of 2 million lives lost (3.6% of total deaths) and 53 million disability-adjusted life years (DALYs) (2.1% of total DALYs).[4]

Another significant threat comes from occupational exposure to hazardous substances at work. One out of six workers in the Netherlands is at risk of developing asthma, chronic obstructive pulmonary disease (COPD), or lung cancer due to such exposure.[5]

These negative health impacts not only affect individuals but also result in societal costs. For example, research from the University of Utrecht found that the total annual medical expenses related to exposure to endocrine-disrupting chemicals in Europe ranges from 46 to 288 billion euros.[6]

In addition to harming our health, chemicals can also have a significant impact on the environment. In Europe, the biodiversity of half of the continent's freshwater bodies is at threat because of chemical pollution.[3] Substances such as flame retardants, per- and polyfluoroalkyl substances (PFAS), pesticides, metals, and polycyclic aromatic hydrocarbons (PAHs) can cause immediate lethal effects as well as long-term chronic impacts on fish, invertebrates, and algae.[7] These chemicals pose a serious risk to the balance and health of aquatic ecosystems.

Why legislation does not guarantee full protection

But what about the strict legislation of hazardous chemicals, why can't we rely on current regulations? It's true that the EU has one of the most comprehensive and protective regulatory frameworks for chemicals worldwide. In 2007, the Registration, Evaluation, and Authorisation of Chemicals (REACH) Regulation was established to assess how chemicals affect humans and the environment. This regulation outlines safety requirements for chemicals produced at volumes of 1 ton per year or more. Chemicals with potentially serious and lasting impacts on human health and the environment are labelled as 'Substances of Very High Concern' (SVHCs). This includes substances linked to cancer (carcinogenic), genetic mutations (mutagenic), or those that are persistent or bio-accumulative. If a substance is identified as an SVHC, it gets added to the Candidate List for potential inclusion in the Authorisation List, which restricts substances not allowed for use in the EU unless authorized by the European Commission (e.g., benzene[8]).

So, why doesn't this legislation guarantee us that all chemicals currently on the market are safe for humans and the environment? Basically there are six reasons:

1. Not all harmful or polluting substances fall under the scope of REACH. Examples of substances not covered include silica, wood dust, and combustion products.

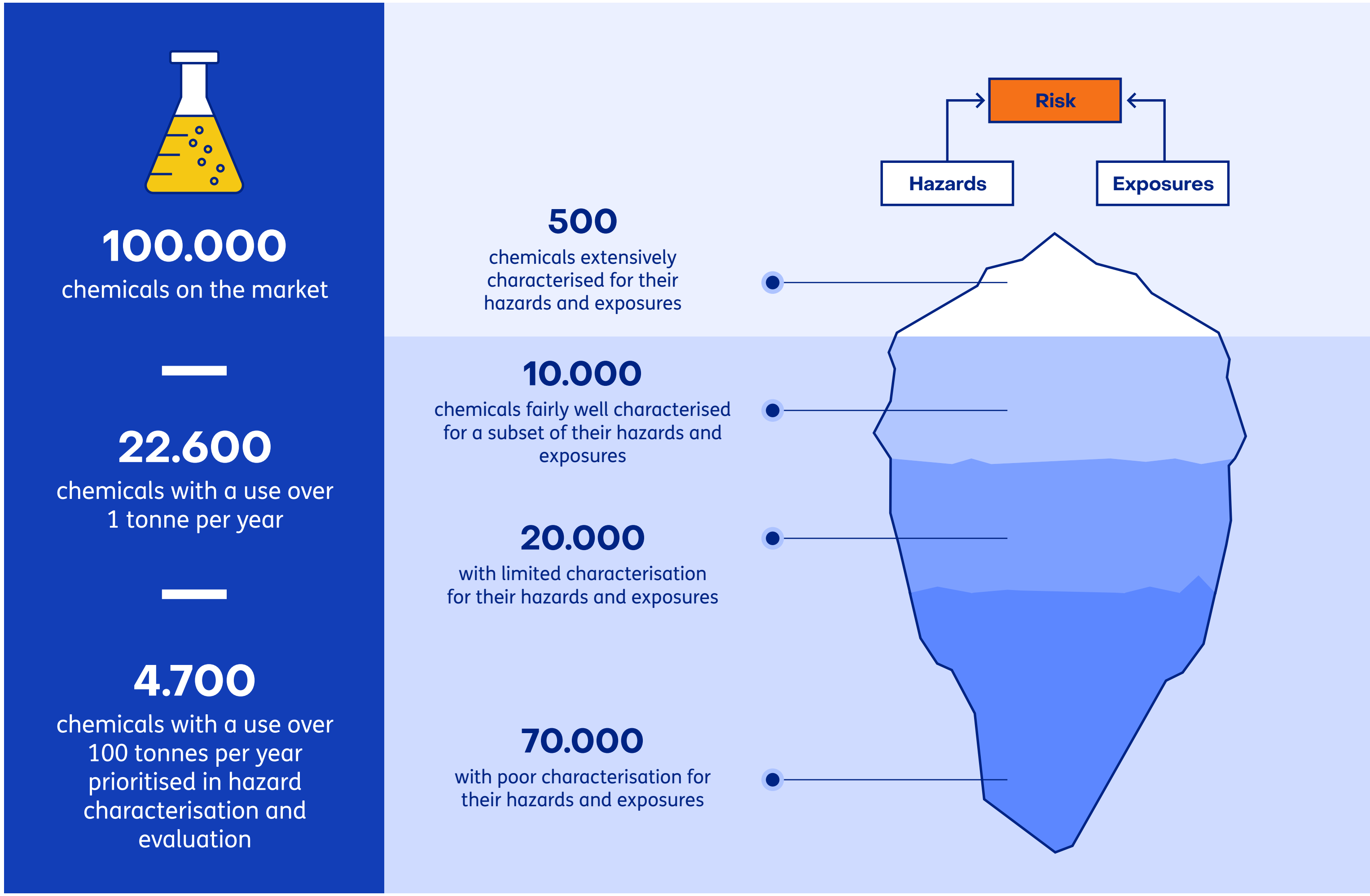
2. Many chemicals were already introduced to the market decades ago, prior to the current chemical regulations. Examples are asbestos or per- and polyfluoroalkyl substances (PFAS - please read box text on PFAS). While the negative health effects of these chemicals became slowly clear, these chemicals were already part of our everyday lives and it will take time to phase out these chemicals.

3. Due to the slow pace of dossier evaluations, a significant number of chemicals on the market haven't undergone safety assessments. Estimates suggest that out of the approximately 23,000 registered chemical substances, around 10,000 substances remained unassessed by the end of 2020, despite REACH having been in place for over 10 years[9].

4. In 2021, the European Chemicals Agency (ECHA) reported that approximately half of the submitted dossiers were incomplete, and around one in ten dossiers had significant flaws[9]. These issues contribute to slowing down the evaluation process.

5. Creating legislation typically takes more time compared to the rapid pace of technological advancements. For instance, technological progress has led to the development of advanced materials like multicomponent nanomaterials, which boast unique properties surpassing those of conventional materials. REACH, however, has for a long time relied on safety assessment methods that were recently challenged by these advanced materials[10, 11]. There is a need to adapt and optimize safety evaluation methods specifically for these materials.

6. In the research and development (R&D) stage, innovations are typically produced in small quantities, often less than 1 ton per year. Consequently, they are not subject to the regulatory requirements of the REACH regulation until they undergo scaling up to larger production volumes.



Only the tip of the iceberg of chemical substances is visible, for which the risks have been sufficiently identified. The risks for the majority of chemicals are not sufficiently clear. Adverse effects of chemicals are often discovered (too) late.

Source: EEA, 2020. The European Environment – State and outlook report

Reducing risks by designing safe and sustainable chemicals

Safe and Sustainable by Design (SSbD)

Safe and Sustainable by Design (SSbD)
As the chemical industry continues to expand, there is a growing demand for new materials and solutions. To address the potential negative side effects associated to chemical or material life cycles on human health and the environment, there is a call for a new approach called Safe and Sustainable by Design (SSbD). SSbD suggests that innovators should think about safety and sustainability right from the start of the innovation process[12, 13].

What does SSbD mean?

Safe and Sustainable by Design is an approach that focuses on considering safety and sustainability early in the process of developing a product, alongside factors like functionality and costs. This helps identify opportunities to enhance safety and sustainability during the initial phases, allowing companies to adjust their products and reduce the likelihood of problems and market failures.
The SSbD assessment involves looking at hazards, release, exposure, risks, environmental sustainability, and social and economic sustainability. The SSbD framework, developed by the Joint Research Centre (JRC) of the EC[14], guides this evaluation.

Traditionally, harmful effects of products are often discovered only after they've been launched in the market, leading to serious issues for society and the environment as well as financial burdens for companies and potential reputational damage. Examples include DDT insecticide, CFCs used as refrigerants, lead in gasoline, asbestos fibers, and BPA used in plastics. SSbD offers a proactive approach to design innovative chemicals and materials. This way, these innovations can provide solutions for societal needs (like the energy transition) while ensuring they are safe and sustainable from the very beginning, avoiding harm to humans or the environment.

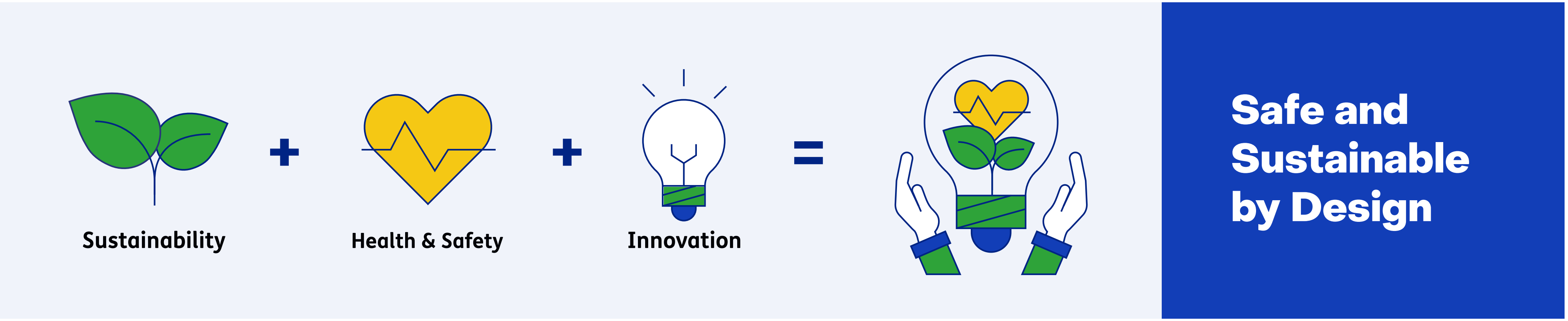


Figure 1: Innovations can provide solutions for societal needs (like the energy transition) while ensuring they are safe and sustainable from the very beginning, avoiding harm to humans or the environment.

Lifecycle thinking is key

A crucial aspect of SSbD is the adoption of life cycle thinking. This means considering the entire life cycle of a chemical, material, or product (as illustrated in Figure 2). Starting from the conceptual design phase, where the idea is first developed, the next steps involve the production or processing of chemicals or materials into final products. Following this, there is the transportation of these products before they are eventually used in various industrial applications or by consumers and eventually end up in waste treatment. By examining the complete life cycle, SSbD ensures that safety and sustainability considerations are integrated at every life cycle stage, from design to production, use and end-of-life.

Figure 2 not only highlights the different life cycle stages of chemicals and products, but it also illustrates the diverse range of stakeholders directly or indirectly involved or impacted by the design, production, use, and end-of-life of chemicals. These stakeholders encompass various entities across the value chain, including raw material suppliers, substance manufacturers, and product manufacturers. Additionally, consumers play a role by influencing the shift towards SSbD through their choices for sustainable products.

Other key stakeholders in this transition include:

1. **Government:** Governments contribute to the transition by establishing import rules, emission regulations, issuing permits, providing incentives, and imposing taxes, among other regulatory measures.

2. **Workers unions:** Labour unions play a role by advocating for safety and sustainability in their demands, ensuring that the well-being of workers is prioritized.

3. **Waste processing sector:** Companies involved in waste processing are crucial stakeholders as they manage the end-of-life stage, dealing with recycling and disposal processes.

4. **Exposed populations:** Consumers of chemical products, end-users of affected ecosystem services.

The collaborative effort of these stakeholders is essential to expedite the shift towards a safe and sustainable industry.

Replacing the old, designing the new

The EU is actively promoting SSbD through the Chemicals Strategy for Sustainability (CSS)[16], launched with the goal of establishing a healthy, sustainable, climate-neutral, and circular economy by 2050.

The strategy aims to achieve this by gradually phasing out, minimizing the use of, and substituting harmful chemical products with safer and less harmful alternatives. The ultimate objective is a complete shift towards SSbD in the development of chemicals, materials, and technologies.

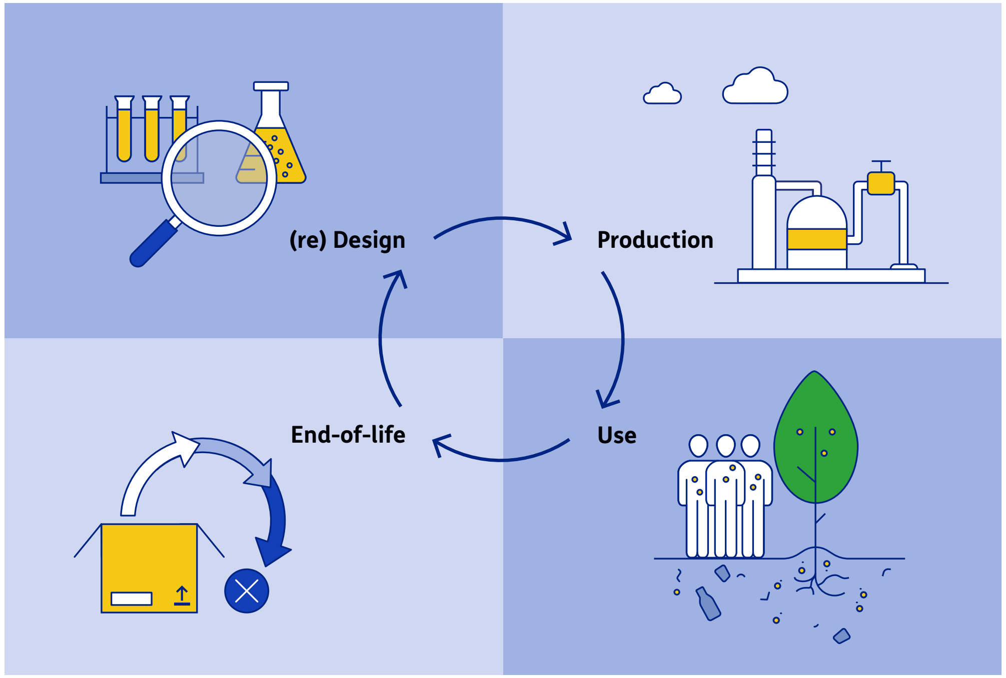


Figure 2. Introducing the life cycle approach with SSbD.[15]

To realize this ambitious goal, two key actions are emphasized:

1. Existing harmful chemicals are targeted for **replacement** with safe and sustainable alternatives.

2. All new chemicals and materials are expected to be **designed** to provide functional and cost-effective solutions for societal needs (like the energy transition) while ensuring they are safe and sustainable from the very beginning, avoiding harm to humans or the environment, aligning with the principles of SSbD[16].

Moreover, the CSS recognizes the need for the existing EU chemicals policy to adapt more swiftly and effectively to challenges posed by hazardous chemicals. One specific initiative within the CSS involves revising the REACH regulation. This revision aims to address issues, including enhancing the identification of substances with critical hazard properties and simplifying the process for EU authorities to assess and restrict larger groups of chemicals that fail to meet the EU's standards for acceptable risk.[17]

The CSS strategy compels chemical innovators, typically concentrated on the functionality of their innovations, to broaden their perspective to encompass not only functionality but also safety and sustainability.

A balancing act

The SSbD methodology helps to prevent harmful chemicals from entering the market. At the same time, SSbD can enhance the innovation process as potentially hazardous substances can be discarded at an earlier stage, avoiding expensive changes later. The challenge is finding the right balance between performance, safety, and sustainability.

Sometimes, to achieve sustainability goals, we might need substances that could be harmful. For instance, in the shift from fossil fuels to renewable energy like wind and solar power, we need new materials for efficient energy conversion[18]. Solar panels, which are cost-effective and can help reduce climate change impacts of energy systems, can still be a concern. Some panels contain harmful chemicals like cadmium and lead, known to cause various health issues.[19]
Another example is the application of harmful PFAS in membranes used for producing clean energy from hydrogen. How do we balance the risks with the benefits in specific applications? This is a key challenge with SSbD.

Proactive approach required

Instead of waiting for legislation, we believe that Safe and Sustainable by Design needs a proactive approach involving the entire supply chain of newly developed chemicals or materials in order to be successful. It starts with everyone agreeing that it's good for both society and industry to design new chemicals in a safe and sustainable way as early as possible in the development.

Imagine if all chemicals entering the market were designed to be safe and sustainable. This would create a much healthier environment. Reduced exposure to harmful chemicals means a healthier and safer living. It also means that workers, especially during the manufacturing of products, would face fewer health risks.

SSbD aligns with the goal of achieving a clean and biodiverse environment within planetary boundaries. Industries, being the creators and producers of chemicals and materials, play a crucial role. Adhering to SSbD principles[20, 21] not only makes them future-proof but also positions them ahead of potential future policies and regulations. This way, industries contribute not only to their own sustainability but also to a healthier and more sustainable future for everyone.

SSbD heralds a brighter future for the industry

The European Chemicals Industry Council (Cefic) recently evaluated the business impacts of the Chemicals Strategy for Sustainability (CSS) on the European chemical industry. According to Cefic, even though the specific policy changes and their implementation timelines remain uncertain, the European chemical economy is projected to face a significant financial impact. It is estimated that the industry could experience a reduction in turnover ranging from 47 to 81 billion euros between 2023 and 2040[22].

This economic impact is attributed to various factors, including the need for additional investments in finding alternative solutions and higher operating expenditures due to increased regulatory requirements.[23] For chemical companies currently involved in innovation, there are limitations imposed by the impending policy changes. These companies may face challenges as they invest in developing products that could potentially be restricted under the new regulations.

By examining potential risks in the early stages, companies can still make adjustments to processes or explore alternative solutions, which is more challenging and costly in later phases of product development. Typically, substantial investments in research, development, and production are made before a product reaches the market. If a recall or phasing out becomes necessary, the profit generated by the product disappears, rendering some or all of the investments obsolete (refer to Figure 3). This also results in damage to the company's reputation.

To minimize the risk of recalls, assessments under the SSbD approach should be conducted at early phases of innovation (i.e. ideation and business case), covering the entire innovation value chain[13]. This proactive approach allows industries to prepare for future regulations and speeds up the innovation process by avoiding expensive design changes at later phases of innovation (pilot scale and commercial scale). Essentially, SSbD serves as a pre-emptive strategy to safeguard against potential issues, ensuring a smoother and more cost-effective development process.

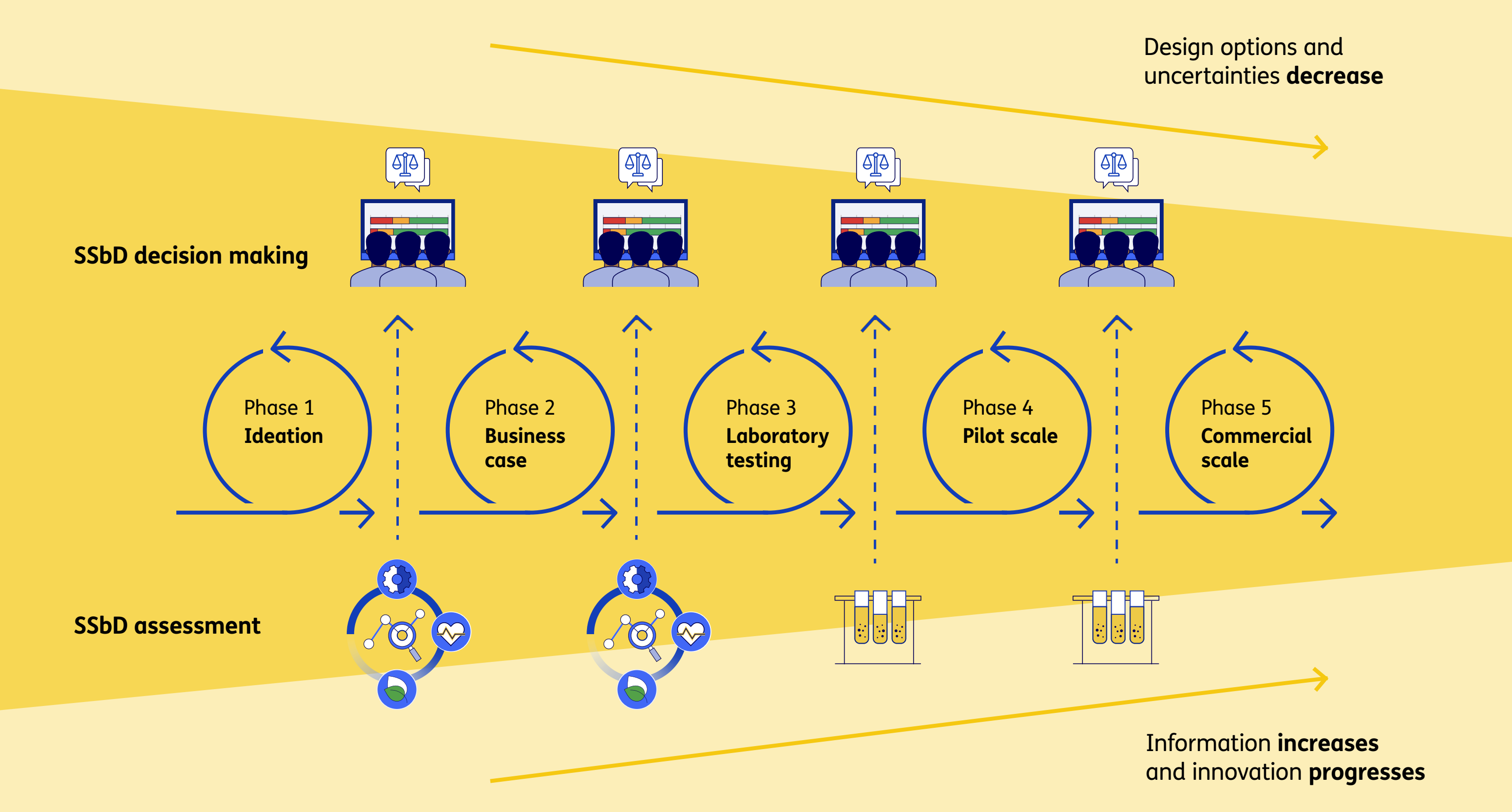


Figure 3: By examining potential risks in the early stages, adjustments can be made to processes or explore alternative solutions, which is more challenging and costly in later phases of product development.

Hurdles that could hinder implementation

The adoption of SSbD represents a path towards a healthier society and environment. However, there are several challenges for industries that hinder the effective implementation of SSbD:

1. **Lack of standardized approach:** There is currently no universally agreed-upon approach for implementing SSbD. Although various SSbD approaches for different sectors are being developed in research projects funded by the European Commission, they are not yet suitable for practical implementation by industries.

2. **Absence of clear legislation:** Existing policy documents are scattered, and there is a need for clear guidance or legislation on how to innovate in a safe and sustainable manner. The framework provided by the Joint Research Centre (JRC) of the EC is a step towards SSbD criteria but lacks practical tools and implementation guidance.

3. **Lack of integration:** The integration of performance, safety, and sustainability is lacking, making decision-making and implementation within a company's innovation process challenging.

4. **Resource constraints:** Companies face limited time and financial resources for product innovation. Implementing SSbD requires an investment at the early stages of product innovation, acting as a potential barrier, especially for Small and Medium-sized Enterprises (SMEs).

5. **Data availability:** SSbD assessments require substantial information on the characteristics of the novel chemical and materials, their associated value chains, and the future developments that determine their social and environmental costs and benefits. This information is often not available or uncertain during early innovation stages.

6. **Supply chain collaboration:** Ensuring the safety and sustainability of chemicals, materials, and products throughout their entire life cycle requires collaboration across the supply chain. Gathering the necessary information for SSbD from different suppliers, manufacturers, distributors, and retailers is challenging.

7. **Multidisciplinary expertise:** SSbD necessitates expertise in multiple fields. A single company, particularly SMEs, lack the in-house expertise or capacity needed to assess the safety and sustainability of substances and products, such as materials science, toxicology, and life cycle assessment.

8. **Paradigm shift:**
   SSbD requires a para-digm shift, necessitating adaptation in internal processes and decision-making within companies. This shift can be challenging for established practices.

Addressing these challenges will be crucial for the successful and widespread implementation of SSbD across industries.

Call for action

We believe that Safe and Sustainable by Design offers a proactive opportunity to design innovative chemicals, materials, and products to provide functional and cost-effective solutions for societal needs, such as those arising from the energy transition. Importantly, SSbD aims to achieve this without causing harm to humans or the environment, embodying the principles of being safe and sustainable by design.

Recognizing that SSbD involves a delicate balancing act between substance functionality, safety, and sustainability, we advocate for an integrated approach.

To support this integrated approach, TNO, in collaboration with stakeholders from manufacturing industry, innovators, researchers, and governments, is developing a multi-criteria Decision Support System (DSS). This system assists industries in evaluating and balancing the risks and benefits during the early stages of their design process. By doing so, we aspire to contribute to the creation of a healthier and more sustainable society.

TNO's Safe and Sustainable Innovation Approach

The four step innovation approach aims to empower companies to take informed decisions based on the integration of health, safety, sustainability, functionality and cost impacts early in the innovation process.

1. **Define product criteria**
   for the intended use of the chemical, material or product.

2. **Quick screening**
   Screening on the selected SSbD aspects (health, safety, sustainability, functionality and cost) Using the SSbD decision support tool, based on available information, data and modelling.

3. **Transparent visualisation and integration**
   of impact on SSbD aspects and visualisation of trade-offs.

4. **Decision making**
   Based on transparent visualisation and scenario testing.
   If needed: more detailed evaluation of one or more SSbD aspects can be performed e.g. by additional data gathering, (in vitro) testing, advanced modelling to reduce uncertainties and allow decision making.

Safe & Sustainable by Design Approach

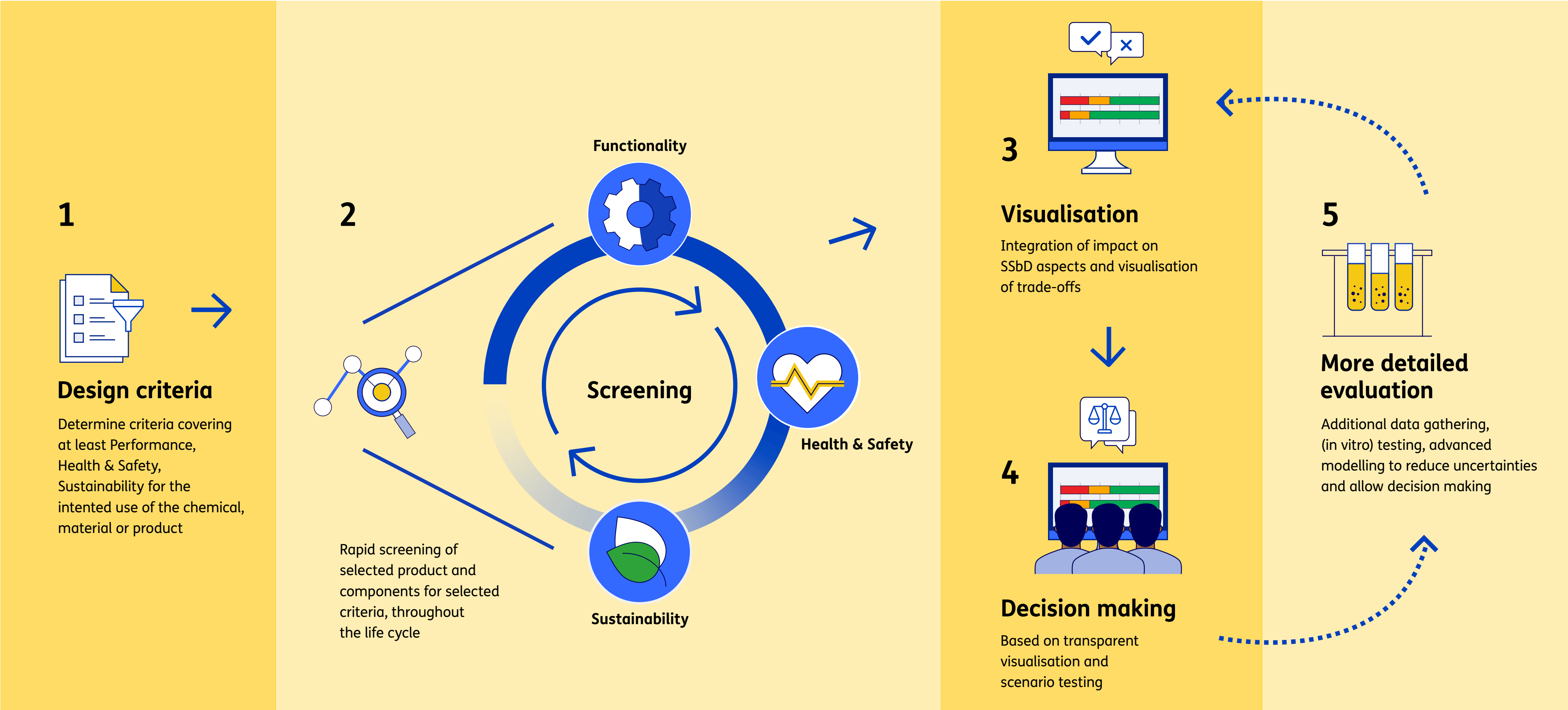
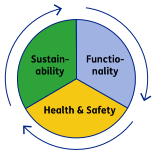


Figure 4. Safe & Sustainable by Design approach to take informed decisions based on the integration of health & safety, sustainability and performance impacts early in the innovation process and throughout the entire life cycle.

To actively advance safer innovation of chemicals, materials, and products, we propose the following actions:

1. Creating a multi-criteria Decision Support System



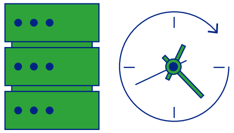
As highlighted earlier, the effective implementation of SSbD demands an integrated approach that evaluates, consolidates, and balances functionality, safety, and sustainability aspects[24], including their uncertainties. Our vision involves creating a multi-criteria Decision Support System (DSS) for industries. This DSS would explore the space of potential future scenarios to anticipate the safety and sustainability profile of chemicals and materials, highlighting relevant functionality, safety, and sustainability factors to reach robust decisions at the early stages of innovation.

The envisioned DSS would cover a range of aspects, including hazard (such as acute and repeated toxicity), process safety (like emissions of harmful substances and worker exposure), environmental sustainability (e.g., ecotoxicity, eutro-phication, energy use, CO2-equivalent emissions, climate change), social and economic sustainability (e.g., forced labour, working hours, local employment).[25–27] The system's output would visually represent the impact of the novel chemical, material, or product on these aspects, indicating areas that need additional effort to minimize undesirable effects.

At TNO, we are actively developing a modular DSS tailored to predict and visualize safety and sustainability impacts. Drawing on our experience in decision support, safety, and sustainability screening, we are applying existing methodologies to support SSbD decision-making[28].

The success of SSbD hinges on collaborative efforts from all stakeholders: Industry transparency regarding the safety and sustainability profile of products, supportive government policies that foster innovation while ensuring safety and sustainability, and responsible consumer choices are vital. TNO advocates for collaboration and interaction among different stakeholders. We commit to participating in international collaborations and projects, acting as a facilitating partner between industry, universities, and government. Through these collaborative efforts, we aim to drive advancements in SSbD and contribute to a safer and more sustainable future.

2. Moving towards automated SSbD predictions



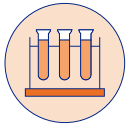
Many current SSbD approaches under development assess performance, safety, and sustainability aspects sequentially, lacking the ability to weigh their impacts. [29–33]
At TNO, we are working towards assessing all relevant aspects in parallel, recognizing their equal importance and interdependence. Given the limited time and resources for innovation in industry, our goal is to have our Decision Support System estimate safety and sustainability aspects in future scenarios based on substance properties or desired functionality using machine learning and computational modelling.

Computational tools are being developed to predict properties or effects of chemical substances[34, 35–39]. Machine learning and artificial intelligence (AI) algorithms can generate new chemical structures meeting desired functionality and safety criteria. However, due to insufficient high-quality data for all relevant aspects (including physicochemical properties, performance parameters, toxicity for humans and the environment, energy consumption, and emissions), data on safety and sustainability must be collected and generated.

TNO is actively collecting physicochemical data for over a million substances and plans to expand toxicity data. The existing data, combined with computational modelling, allows us to fill data gaps, replace substances of concern with safer alternatives, and predict the toxicity of novel substances. The expanded TNO data set also provides the opportunity to generate novel chemical structures based on performance by exploring the use of advanced computational tools such as machine learning.

To accelerate data collection and tailor the SSbD tool to specific industry needs, TNO calls for close collaboration with Database for SSbD predictions. industry partners. Companies benefit from this collaboration by receiving decision support for their innovation, including identifying safety and sustainability alerts and options for mitigation. Through this collaborative effort, we aim to advance the SSbD tool and facilitate a more sustainable and safer innovation process.

3. Using NAMs to accelerate SSbD assessment



Human safety aspects, a crucial pillar in SSbD, currently undergo a full hazard assessment late in the product market launch to comply with regulations such as REACH. However, this process is time-consuming, resource-intensive, relies heavily on animal studies, and may lead to unexpected toxicity issues. To address these challenges and accelerate non-animal hazard assessment, New Approach Methodologies (NAMs) are proposed. NAMs are technologies or methodologies that provide information on chemical or material hazard, exposure, and risk assessment without using animals.

In the context of SSbD, NAMs can rapidly screen for potential hazard alerts in the early design phase, minimizing the risk of failed market approvals. TNO suggests a testing strategy for each relevant human health endpoint within SSbD, emphasizing the need for an independent and accessible hazard screening infrastructure in the Netherlands.

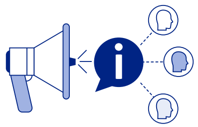
This infrastructure would facilitate quick screening of innovative chemicals and materials for potential human and environmental hazards. The data generated could serve two purposes: assessing potential hazards for companies and training machine learning models to automate SSbD.

TNO calls for collaboration with universities and companies to establish this infrastructure, combining chemical and material characterization with high-throughput and high-content hazard screening methods. The collaboration aims to develop and implement innovative screening techniques.

Similarly, in the realm of sustainability, there is a need for Life Cycle Assessment (LCA) predictive tools that can rapidly screen for potential sustainability impacts. TNO is working to advance existing initiatives that use machine learning and high-throughput screening[40, 41] for LCA, moving towards implementation in an integrated SSbD approach. Collaborations with universities, companies, and regulatory bodies are sought to accelerate and enhance safety and sustainability screening for complex, innovative materials.

TNO also seeks cooperation with regulatory bodies to pave the way for the acceptance and implementation of NAMs, initially for SSbD and subsequently for regulatory risk assessment.

4. Increasing awareness and transparency



To successfully transition towards safer and more sustainable innovations, it is essential for industry, governments, regulators, and consumers to be aware of the societal need for change. Each stakeholder group must understand and address the needs of others, fostering a collaborative environment in line with the EU Chemical Strategy for Sustainability.

TNO advocates for increased awareness and transparency regarding SSbD and its impacts. A growing number of consumers are willing to pay more for sustainable products, but they often struggle to find relevant and reliable information. To address this, industries should be more transparent about the safety and sustainability profile of their products.

Upcoming regulations, such as the corporate sustainability reporting directive (CSRD) and the Ecodesign for Sustainable Products Regulation (ESPR), which includes a Digital Product Passport with information on products' environmental sustainability, will contribute to this transparency. Implementing SSbD now positions industries to be prepared for these impending regulations.

Governments can play a role by enabling an SSbD label, allowing consumers to make informed decisions and choose safe and sustainable products. TNO suggests that education and training on SSbD are crucial components of this transition. Universities should integrate SSbD into their curricula to educate future innovators.

Through these concerted efforts, SSbD can become a success, contributing to responsible innovation and consumption. Collaborative actions will not only benefit the environment but also align with the evolving expectations and preferences of conscious consumers. Together, stakeholders can drive positive change and pave the way for a more sustainable and healthier future.

Imagine the future of products that are safe and sustainable by design

Imagine wanting to develop a ground-breaking product to expedite the energy transition. For example: nanostructures designed to efficiently convert solar energy into electrical power. Now, envision having the capability to identify and transparently visualize potential safety or sustainability concerns for all the candidate substances involved alongside their functionality and costs at the early phase of product innovation.

As a motivated product developer aiming to drive the energy transition, you possess knowledge of nanomaterials and nanostructures designed to convert solar energy into electrical power. With several different nanostructures in mind, varying in chemical composition, crystallinity, size, and shape, your challenge lies in lacking information on the toxicity and sustainability profiles of these novel structures. A selection based solely on functionality and costs might result in product failure later due to unforeseen toxicity or sustainability concerns. Fortunately, you have access to the TNO SSbD tool. This online tool prompts you to input details about the physicochemical properties of your nanostructures, their functionality, and intended use. Depending on the phase of innovation and the SSbD aspects that are of interest to the user, the SSbD tool performs a qualitative screening estimation relying on little data. Leveraging machine learning and Quantitative Structure Activity Relationships (QSAR) models, the SSbD tool estimates potential adverse effects for both humans and the environment (e.g., persistency, mobility, and toxicity).

Simultaneously, it conducts a prospective life-cycle assessment (LCA) using the information provided, predicting the impact on sustainability aspects throughout the structures' life cycle, such as resource use, climate change, water use, energy demand and social and economic aspects.

All these steps occur seamlessly and in parallel within the TNO SSbD screening tool. The output is a comprehensive visualization of the functionality, safety, and sustainability profile of each nanostructure, complete with uncertainty and variability indicators. The screening tool identifies specific safety or sustainability aspects that demand additional attention or action, providing a quick overview of which nanostructures trigger hazard or sustainability alerts and the associated aspects within these parameters by using multi-object optimization to quantify the optimal design given all relevant SSbD aspects. In addition, it identifies which people should connect to discuss the trade-offs between SSbD aspects. This information guides you in rejecting certain nanostructures for further development. From the remaining options, you can confidently select the most promising nanostructure candidates for further development and prototyping, while the tool provides you with recommendations on more detailed evaluation of one or more SSbD aspects e.g. by additional data gathering, (in vitro) testing, advanced modelling to reduce uncertainties and allow decision making at later innovation stages. By leveraging the SSbD tool, companies can expedite their innovation process, avoid costly design changes, innovate responsibly, and actively contribute to a healthy, sustainable society.

References

1. MaterialenNL Platform. *Nationale Agenda Materialen, Accelerating Materials Technologies.* (2020).
2. UNEP. *Global Chemicals Outlook II: From Legacies to Innovative Solutions.* (2019).
3. European Environment Agency. *Chemicals for a Sustainable Future: Report of the EEA Scientific Committee Seminar.* https://www.eea.europa.eu/about-us/governance/scientific-committee/reports/chemicals-for-a-sustainable-future/at_download/file (2017).
4. WHO. *The Public Health Impact of Chemicals: Knows and Unknows. Data addendum for 2019.* https://www.who.int/publications/i/item/WHO-HEP-ECH-EHD-21.01 (2016).
5. Ministerie van Sociale Zaken en Werkgelegenheid, (SZW);, TNO; & BKB. *Programma Preventie beroepsziekten.* https://www.arboportaal.nl/documenten/publicatie/2023/01/19/programma-preventie-beroepsziekten (2023).
6. Rijk, I., van Duursen, M. & van den Berg, M. *Health costs that may be associated with Endocrine Disrupting Chemicals.* (2016).
7. Malaj, E. *et al.* Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. *Proc. Natl. Acad. Sci.* 111, 9549–9554 (2014).
8. ECHA. PIC - Prior Informed Consent Regulation. https://echa.europa.eu/nl/information-on-chemicals/pic/chemicals?p_p_id=pic_ChemicalsPortlet&p_p_lifecycle=0&p_p_state=normal&p_p_mode=view&_pic_ChemicalsPortlet_useCategory2=false&_pic_ChemicalsPortlet_container=aeContainer&_pic_ChemicalsPortlet_useCateg.
9. Persson, L. *et al.* Outside the Safe Operating Space of the Planetary Boundary for Novel Entities. *Environ. Sci. Technol.* 56, 1510–1521 (2022).
10. Johnston, L. J., Gonzalez-Rojano, N., Wilkinson, K. J. & Xing, B. Key challenges for evaluation of the safety of engineered nanomaterials. *NanoImpact* 18, 100219 (2020).
11. Schwirn, K., Voelker, D., Galert, W., Quik, J. & Tietjen, L. Environmental Risk Assessment of Nanomaterials in the Light of New Obligations Under the REACH Regulation: Which Challenges Remain and How to Approach Them? *Integr. Environ. Assess. Manag.* 16, 706–717 (2020).
12. OECD. *Safe(r) and Sustainable Innovation Approach (SSIA).* https://oe.cd/ssia (2023).
13. OECD. Sustainability and Safe and Sustainable by Design: Working Descriptions for the Safer Innovation Approach. 1–12 (2022).
14. Caldeira *et al.* Safe and Sustainable chemicals by design chemicals and materials. 1–185 (2022).
15. Malyska, A. *Innovation Plan for safe and sustainable Chemicals and Materials.* doi:10.2777/876851.
16. European Commission. Chemicals Strategy for Sustainability Towards a Toxic-Free Environment. 25 at (2020).
17. EC. Recommendation for safe and sustainable chemicals published.
18. S&P Global. What is Energy Transition? https://www.spglobal.com/en/research-insights/articles/what-is-energy-transition#:~:text=Energy transition refers to the,well as lithium-ion batteries. (2020).
19. Shellenberger, M. If solar panels are so clean, why do they produce so much toxic waste? https://www.forbes.com/sites/michaelshellenberger/2018/05/23/if-solar-panels-are-so-clean-why-do-they-produce-so-much-toxic-waste/?sh=6e4d594121cc.
20. Shandilya, N. *et al.* Perspective on a risk-based roadmap towards the implementation of the safe innovation approach for industry. *NanoImpact* 20, 100258 (2020).
21. Ministerie van infrastructuur en waterstaat. *Informatiekaart Safe-and-Sustainable-by-Design.* (2022).
22. Ricardo. Economic Analysis of the Impacts of the Chemicals Strategy for Sustainability, ED 14790, Issue number 1. 157 (2021).
23. ECHA. Candidate list obligations.
24. Subramanian, V. *et al.* Approaches to implement safe by design in early product design through combining risk assessment and Life Cycle Assessment. *Chemosphere* 311, 137080 (2023).
25. Caldeira, C. et al. *Safe and Sustainable by Design chemicals and materials - Application of the SSbD framework to case studies.* (2023). doi:10.2760/769211.

26. Tulus, V., Pérez-Ramírez, J. & Guillén-Gosálbez, G. Planetary metrics for the absolute environmental sustainability assessment of chemicals. *Green Chem.* 23, 9881–9893 (2021).

27. Fantke, P., Huang, L., Overcash, M., Griffing, E. & Jolliet, O. Life cycle based alternatives assessment (LCAA) for chemical substitution. *Green Chem.* 22, 6008–6024 (2020).

28. Doornbos, R. DAARIUS methodology. https://esi.nl/research/output/methods/daarius-methodology.

29. World Business Council for Sustainable Development. Chemical Industry Methodology for Portfolio Sustainability Assessments (PSA). 1–46 at (2018).

30. Reihlen, A; Bunke, D; Gruhlke, A; Gross, R; Blum, C. Guide on Sustainable Chemicals A decision tool for substance manufacturers, formulators and end users of chemicals. 76 at https://doi.org/ISSN 2363-832X (2016).

31. Sanchez Jiminez, A. et al. Safe(r) by design guidelines for the nanotechnology industry. 25, (2022).

32. Falinski, M. M. et al. A framework for sustainable nanomaterial selection and design based on performance, hazard, and economic considerations. *Nat. Nanotechnol.* 13, 708–714 (2018).

33. CEFIC. Safe and Sustainable- a Guidance To Unleash the Transformative Power of Innovation. (2024).

34. Silva, M. & Kwok, R. K.-H. Use of computational toxicology models to predict toxicological points of departure: A case study with triazine herbicides. *Birth defects Res.* 115, 525–544 (2023).

35. Filer, D. L., Hoffman, K., Sargis, R. M., Trasande, L. & Kassotis, C. D. On the Utility of ToxCast-Based Predictive Models to Evaluate Potential Metabolic Disruption by Environmental Chemicals. *Environ. Health Perspect.* 130, 57005 (2022).

36. Loizou, G., McNally, K., Paini, A. & Hogg, A. Derivation of a Human In Vivo Benchmark Dose for Bisphenol A from ToxCast In Vitro Concentration Response Data Using a Computational Workflow for Probabilistic Quantitative In Vitro to In Vivo Extrapolation. *Front. Pharmacol.* 12, 754408 (2021).

37. Nicolas, C. I. et al. Estimating provisional margins of exposure for data-poor chemicals using high-throughput computational methods. *Front. Pharmacol.* 13, 980747 (2022).

38. Green, A. J. et al. Leveraging high-throughput screening data, deep neural networks, and conditional generative adversarial networks to advance predictive toxicology. *PLoS Comput. Biol.* 17, e1009135 (2021).

39. Lane, T. R., Harris, J., Urbina, F. & Ekins, S. Comparing LD(50)/LC(50) Machine Learning Models for Multiple Species. *J. Chem. Heal. Saf.* 30, 83–97 (2023).

40. Zhu, X., Ho, C.-H. & Wang, X. Application of Life Cycle Assessment and Machine Learning for High-Throughput Screening of Green Chemical Substitutes. *ACS Sustain. Chem. Eng.* 8, 11141–11151 (2020).

41. Song, R., Keller, A. A. & Suh, S. Rapid Life-Cycle Impact Screening Using Artificial Neural Networks. *Environ. Sci. Technol.* 51, 10777–10785 (2017).

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